

REMARKS/ARGUMENTS**I. Preliminary Remarks**

Applicant, through the undersigned attorney wishes to thank the Examiner for the courtesy shown to the undersigned during the telephonic interview conducted April 21, 2004. As discussed at that Interview Applicant hereby amends claims 7-9 and further submits new claims 11-14 in order to clarify the subject matter of the invention. These amendments do not introduce new matter into the application and place the claims in a form in which the method steps correlate with the unexpected improvements in the prevention of self-annealing disclosed in the specification.

Accordingly, claims 7-10 present the invention as a method forming a random mixture of oligonucleotides which is resistant to self-annealing comprising the steps of (1) selecting a random mixture of oligonucleotides which are 6-mers to 8-mers and (2) drying the mixture. New claims 11-14 present the subject matter of the invention in Jepson format wherein the invention provides an improvement in forming random mixtures of oligonucleotides comprising the same two steps.

The present invention relates to the discovery (1) that there is a self-annealing problem with dried primers and (2) that the solution to that problem is the use of shorter dried primers. Accordingly, the invention provides methods of forming random mixtures of oligonucleotides which are resistant to self-annealing and relates to the recognition that the self-annealing problem is specific to 9-mers (and longer oligonucleotides) used in dried kits and does not represent such a problem with shorter dried primers.

II. The Outstanding Rejections.

Claims 7-10 stand rejected under 35 U.S.C. §112 (second paragraph) as indefinite.

Claims 7-10 stand rejected under 35 U.S.C. §103(a) Over Godiska, U.S. 5,759,804 in view of Shen EP 0 726 310.

III. The Rejections Under 35 U.S.C. § 112 (second paragraph) Should be Withdrawn.

As discussed at the Interview, the amended claims are in a form in which the method steps correlate with the unexpected improvements in the prevention of self-annealing disclosed in the specification. Further, as also discussed, dCTP incorporation described in the Examples is merely an assay measuring self-annealing and is not an element of the invention. Accordingly, the rejections under 35 U.S.C. § 112 (second paragraph) should be withdrawn.

IV. The Rejections Under 35 U.S.C. § 103(a) Should be Withdrawn.

As discussed at the Interview, Applicant's invention is not anticipated by any of the prior art. As further discussed at the Interview, the application Examples demonstrate a critical and unexpected difference in self-priming activity and labeling intensity between 6-8 mers and 9-mers and there is no suggestion in the art that such a difference could occur. Accordingly, the obviousness rejection under 35 U.S.C. §103(a) should be withdrawn because the art fails to teach the desirability of short primers (6-8 mers) in a dried primer system or that 6-mers to 8-mers would behave differently with respect to self-priming activity and labeling intensity than do 9-mers.

More specifically, Godiska discloses liquid 6-mers but fails to teach (1) that the selection of 6-mers to 8-mers constitutes a critical range or (2) that short primers (6-8 mers) would be desirable in a dried primer system. While Godiska discloses a random mixture of

6-mers and other ingredients the Examiner acknowledges that Godiska does not teach a labeling composition in a dry state. Moreover, there is nothing in Godiska that teaches that the selection of 6-mers to 8-mers is important in either the liquid or freeze dried state to reduce self-annealing. In fact, self annealing is not mentioned at all!

Meanwhile, Shen discloses dried 48-mer and 22-mer primers but fails to suggest that such dried primers should be shortened (or alternatively any reason why the short primers of Godiska should be dried). This is because the prior art generally taught that longer primers were preferred because longer primers have higher melting temperatures and are thus more specific.

Moreover, Shen acknowledges that "whether a particular composition will function to preserve biological activity for a particular biologically active material is not a priori predictable" (page 4, lines 36-37) and only discloses freeze-drying as an "option" (Pg. 5, Lines 14-15). In addition, Shen fails to provide any reason why the primers of Godiska should be dried given the fact that shorter primers were thought to be inherently more stable and that there was no reason to believe that the shorter Godiska primers would benefit from being in freeze-dried kits.

For these reasons, the rejections under 35 U.S.C. §103 (a) should properly be withdrawn. Should the Examiner have any questions or comments of form on substance, she is encouraged to contact the undersigned attorney.

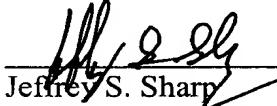
CONCLUSION

In view of the foregoing remarks, claims 7-10 are believed to be in condition for allowance. Favorable reconsideration and allowance of the application is respectfully requested. Should the Examiner have any concerns of either form or substance she is encouraged to contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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